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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/634,252		Douglas P. Cerretti	03260.0051	3642

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EXAMINER	
MOORE, WILLIAM W	
ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/634,252	CERRETTI, DOUGLAS P.	
	Examiner	Art Unit	
	William W. Moore	1652	

-- The MAILING DATE of this c mmunication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,21-23 and 30-46* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15,16,21-23,30-32,34-40,42 and 44-46* is/are rejected.

7)☒ Claim(s) *33,41 and 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Information Disclosure Statement

Applicant's Supplemental Information Disclosure Statement, Paper No. 13 filed August 22, 2002, is hereby acknowledged. The published patent applications of Lopez-Ortin et al. and Sheppard et al., respectively Publication Nos. US 2002/0001840 and US 2002/0072102 submitted with Paper No. 13, are not prior art to an invention claimed herein. This rejection is not made final because both the published EST sequence of Hillier et al. and the U.S. Patent No. 6,265,199 to Sheppard et al. submitted with Paper No. 13 are available as prior art and were published before Paper No. 11 was mailed, where both can be applied below to claim 15 as it had appeared before, as well as subsequent to, the amendments of Paper No. 13.

Response to Amendment

Applicant's Amendment B, Paper No. 12 filed August 22, 2002, has been entered. The cancellation of claims 17, 18, and 24-29, and the amendments to claims 15, 22, 23 overcome the objection of record of claim 22 and the rejection of record of claims 15, 22 and 25 under 35 U.S.C. §112, second paragraph. In view of the amendments of Paper No. 12, Applicant's arguments at pages 14-16 therein, and a separate determination of patentability of a polypeptide comprising corresponding disintegrin domain(s) of the zdint1 polypeptide as reflected by the claims of Sheppard et al.('199), the rejections of record of claims 15, 16, and 21-23 under 35 U.S.C. §101 and 35 U.S.C. §112, first paragraph, for lack enablement as to use and as to making are withdrawn and they are not applied to the new claims 30-33 and 38-46. The rejections of record previously applied to claims 15, 16, and 21-23 under 35 U.S.C. §§101 and 112, first paragraph, for lack of utility, as well as for lack of enablement and for lack of an adequate written description are, however, now applied to the new claims 34-37 herein.

Claim Rejections - 35 USC § 101

35 U.S.C. §101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 34-37 are rejected for reasons of record under 35 U.S.C. §101 because the claimed invention lacks patentable utility.

Applicant's arguments filed August 22, 2002, have been fully considered but they are not persuasive with respect to the new claims 34-37 which permit an encoding nucleic acid molecule to differ significantly from SEQ ID NO:2 herein, thus vitiating the utility argued by Applicant where such molecules, even those of claim 36 which may differ in nucleotide sequence extensively elsewhere, may neither serve as tissue-specific markers nor encode a domain having the activity of a SVPH3-17/ADAM23, or the prior art zdint1, disintegrin domain. A claimed invention must posses a specific, substantial and credible *in vitro* or *in vivo* utility. While the disclosed SEQ ID NO:2 encodes a native human protein comprising a disintegrin domain, the specification provides no **specific** *in vitro* utility that is also **substantial** for a nucleic acid encoding an undisclosed SVPH3-17/ADAM-23 variant. A method of use of a material for further research to determine, e.g., its specific biological role, thus identifying or confirming a "real world" context for its use, cannot be considered to be a "substantial utility". *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). Nothing in the specification indicates that Applicant knew of any specific utility for a nucleic acid sequence encoding a variant at the time the application was filed. This rejection may be overcome by canceling the rejected claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-37 are also rejected under 35 U.S.C. §112, first paragraph. Specifically, since the claimed invention is not supported by either a **specific** asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to **use** the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-37 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant's arguments filed August 22, 2002, have been fully considered but they are not persuasive with respect to the new claims 34-47 which permit an encoding nucleic acid molecule to differ significantly from SEQ ID NO:2 herein, thus are not supported by Applicant's arguments where such molecules may differ significantly in sequence from the nucleic acid sequence species set forth in SEQ ID NO:2 and genera of nucleic acid sequences isocoding with SEQ ID NO:2. "While one does not need to have carried out one's invention before filing a patent application, one does need to be able to describe that invention with particularity" to satisfy the description requirement of the first paragraph of 35 U.S.C. §112. *Fiers v. Revel v. Sugano*, 25 USPQ2d 1601, 1605 (Fed. Cir. 1993). Yet the specification fails to exemplify or describe the design or preparation of the subject matters of such variant nucleic acid sequences encoding polypeptides that either generally diverge from the overall amino acid sequence of SEQ ID NO:4 or diverge regionally from the amino acid sequence of SEQ ID NO:4, nor is there any indication in the specification where the encoded amino acid sequence might diverge or how it might diverge from the amino acid sequence of SEQ ID NO:4. Similarly, the specification fails

to disclose or to suggest nucleic acid sequences encoding other polypeptides that might be, for example, allelic variants or splice variants of the SVPH3-17/ADAM-23 polypeptide of SEQ ID NO:4. As noted in Paper No. 11 mailed March 15, 2002, if 10% of nucleic acid sequence deviations occur in first codon positions, the overall amino acid sequence may encode generic proteins differing at as many as 30% of the positions in the amino acid sequence of SEQ ID NO:4 and the specification provides not even a suggestion as to where the first alteration in amino acid sequence should occur.

The Court of Appeals for the Federal Circuit held that a claimed invention must be described with such "relevant identifying characteristic[s]" that the public could know that the inventor possessed the invention at the time an application for patent was filed, rather than by a mere "result that one might achieve if one had made that invention". *University of California v. Eli Lilly*, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). Indeed, the claims rejected herein are, like the claims invalidated by the appellate panel in *University of California v. Eli Lilly*, designed to embrace other, as yet unknown, human metalloprotease-disintegrins and metalloprotease-disintegrins of other mammalian species as evidenced by the prior art made of record herewith. Nothing demonstrates that, at the time the specification was filed, Applicant was "able to envision" enough of the structure of a nucleic acid sequence encoding any of these undisclosed generic proteins to provide the public with identifying "characteristics [that] sufficiently distinguish it . . . from other materials". *Fiers*, 25 USPQ2d at 1604 (citing *Amgen, Inc. v. Chugai Pharmaceutical Co.*, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991). The specification's treatment of the claimed subject matter is considered to be entirely prospective where skilled artisans in the relevant field of molecular biology could not predict the structure, or other properties, of the claimed products. This rejection may be overcome by canceling the rejected claims.

Claims 34-37 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for preparation of nucleic acid sequences encoding a metalloprotease-disintegrin of SEQ ID NO:4, as well as nucleic acid sequences encoding fragments of SEQ ID NO:4 having disintegrin activity,

does not reasonably provide enablement for preparation of nucleic acid sequences encoding a polypeptide having an amino acid sequence that diverges, by virtue of amino acid substitutions, deletions and insertions, or combinations thereof at as many as 30% of the amino acid positions from that of SEQ ID NO:4. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant's arguments filed August 22, 2002, have been fully considered but they are not persuasive with respect to the new claims 34-37 which permit an encoding nucleic acid molecule to differ significantly from SEQ ID NO:2 herein, thus are not supported by Applicant's arguments where such molecules may differ significantly in sequence from the nucleic acid sequence set forth in SEQ ID NO:2 and the genus of nucleic acid sequences isocoding with SEQ ID NO:2. As noted in Paper No. 11 mailed March 15, 2002, the specification cannot support the degree of amino acid insertions, deletions, or substitutions anywhere, in any combination or any pattern, in the amino acid sequence set forth in SEQ ID NO:4. It is well settled that 35 U.S.C. §112, first paragraph, requires that a patent disclosure be sufficiently enabling to allow one of skill in the art to practice the invention as claimed without undue experimentation and that unpredictability in an attempt to practice a claimed invention is a significant factor supporting a rejection under 35 U.S.C. §112, first paragraph, for non-enablement. See, *In re Wands*, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (recognizing and applying the "*Forman*" factors). Cf., *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986) (citing eight factors used to analyze enablement). Mere sequence perturbation will not enable the design and preparation of nucleotide sequences encoding a myriad of divergent proteases and provide the public with a nucleotide sequence encoding a protease that retains its native function and the standard set by the CCPA, the precursor of the Court of Appeals for the Federal Circuit, is not to "make and screen" any and all possible alterations because a reasonable correlation must

exist between the scope asserted in the claimed subject matter and the scope of guidance the specification provides. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 25 (CCPA 1970) (scope of enablement varies inversely with the degree of unpredictability of factors involved in physiological activity of small peptide hormone); **see also**, *Ex parte Maizel*, 27 USPQ2d 1662, 1665 (Bd. Pat. App. & Int. 1992) (functional equivalency of divergent gene products not supported by disclosure only of a single B-cell growth factor allele). The Federal Circuit approved this standard set by the CCPA in *Genentech, Inc. v. Novo-Nordisk A/S*, 42 USPQ2d 1001 (Fed. Cir. 1997). Applying the "*Forman*" factors discussed in *Wands*, ***supra***, to Applicant's disclosure, it is apparent that:

a) the specification lacks adequate, specific, guidance for altering DNA sequences coding for the SVPH3-17/ADAM12 molecule set forth in SEQ ID NO:4 to the extent recited in the claims,

b) the specification lacks working examples wherein an SVPH3-17/ADAM-23 metalloprotease-encoding nucleic acid sequence is altered to the extent recited in the claims,

c) in view of the prior art publications of record herein, the state of the art and level of skill in the art do not support such alteration, and,

d) unpredictability exists in the art where no other metalloprotease-disintegrin of the class represented by the amino acid sequence of SEQ ID NO:4 has had as many as 250 amino acids specifically identified for concurrent modification.

Thus the present specification cannot be considered to support the scope of subject matters embraced by claims 34-37 even when taken in combination with teachings available in the prior art. This rejection may be overcome by canceling the rejected claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. §102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. §102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. §122(b). Therefore, this application is examined under 35 U.S.C. §102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. §102(e)).

Claims 15, 31, 31, 38 and 39 are rejected under 35 U.S.C. §102(a) as being anticipated by Hillier et al., EST database Accession No. 185722 and the GenBank database Accession No. R15308.

The EST sequence of Hillier et al., submitted with Paper No. 13, anticipates a nucleic acid molecule of clause (e) of the amended claim 15 because it provides an uninterrupted open reading frame encoding the region of SEQ ID NO:4 herein from amino acid position 489 to position 569, inclusive, and likewise meets the structural and functional limitations of claims 31, 38 and 39.

Claims 15, 16, 21-23, 30-32, 34-40, 42 and 44-46 are rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,265,199 to Sheppard et al.

Submitted with Paper No. 13, Sheppard et al. is available as prior art in view of the July 10, 1998, filing date of the application that issued as the '199 patent. Sheppard et al. disclose a SEQ ID NO:1, a nucleic acid sequence encoding the patent's SEQ ID NO:2 which is a 696-amino acid metalloprotease-disintegrin. Save for two relative amino acid substitutions at positions 306 and 405 within the catalytic domain of SEQ ID NO:4 herein, the patent's SEQ ID NO:2 is identical to the amino sequence of SEQ ID NO:4 herein from position 132 through position 786, inclusive, lacking the initial 131 amino acids and the final 48 amino acids of SEQ ID NO:4 herein either due to a failure of the primer-extension procedure used to screen a fetal brain cDNA library disclosed in Example 1 of the patent or to an alternative splicing of a nuclear RNA transcript. Thus the nucleic acid sequence of SEQ ID NO:1 of Sheppard et al. meets the structural and functional limitations of claims 15, 31, 32, 34-40, 42 and 44-46 herein. The further disclosure of Sheppard et al. of preparation of an expression vector comprising a nucleic acid meeting limitations of claim 15 as amended herein, the transformation of a host cell with the

vector, and the recombinant expression of an encoded, disintegrin domain-comprising polypeptide, meets the limitations of claims 16, 21-23 and 30 herein.

Conclusion

Claims 33, 41 and 43 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to William W. Moore whose telephone number is 703.308.0583. The examiner can normally be reached from 8:00AM-6:30PM EST on Mondays, Wednesdays, and Fridays and from 11:30AM-6:00PM EST on Tuesdays and Thursdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy can be reached at 703.308.3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703.308.4242 for regular communications and 703.308.0294 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703.308.0196.

William W. Moore
October 22, 2002

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